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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/472,691 12/27/99 HERMISTON

T ONYX1022

EXAMINER

HM22/0201

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ART UNIT

PAPER NUMBER

1633

DATE MAILED:

02/01/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/472,691

Applicant(s)

HERMISTON ET AL.

Examiner

Eleanor Sorbello

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 November 2000.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1- 3 and 5-10 and 12-14 is/are rejected.
- 7) ☐ Claim(s) 4 and 11 is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____.

Response to amendment

1. Applicant's amendment and response to the official Office Action mailed May 05, 2000 as Paper No. 4, has been received and filed on November 14, 2000 as Paper No. 8B. Claims 1, 5, and 12 have been amended, and claims 13 and 14 have been added. Claims 1-14 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's argument.

2. Applicant's arguments are addressed below on a per section basis. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 10 and 11 stand rejected under 35 USC § 112, first paragraph for reasons of record. Applicant's arguments have been fully considered but they are not persuasive.

Claims 10 and 11 are directed to a method for treating a mammal with a neoplastic condition by administering constructs of the instant invention in therapeutically effective dosages, and further limitations comprising administering the aforementioned together with a chemotherapeutic or an immunosuppressive.

As stated in the FOAM, administering a gene construct falls in the realm of gene therapy. It additionally falls in the realm of cancer therapy as it is directed to the treatment of a neoplastic condition. As discussed in the FOAM, the administration of a

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gene in any construct is unpredictable, and the art is not established wherein results can be extrapolated and therefore predicted. Applicants pointed examiner's attention to page 18-22 of the specification, wherein applicants contend that methodology to gene therapy were given in detail. However, examiner contends that the specification taught gene therapy application only by prophetic consideration. Therefore because the Office reasonably set forth reasoning to make a prima facie case of lack of enablement, the burden is on the applicant to provide evidence that such a construct was administered to an art accepted model, wherein a neoplastic condition was treated.

Applicants have argued that the working examples provided by applicants wherein *in vitro* examples of cell lines to which the constructs were administered and which provided sufficient evidence for therapy. Applicants examples of cultured cells to which constructs were administered, wherein the inserted CD and TNF genes were expressed does not, in examiner's view provide evidence that therapy of a neoplastic condition will take place, due to the unpredictability in the art. *In vitro* results cannot predictably be extrapolated to *in vivo* results.

Applicants have argued that the art of introducing a gene and obtaining a therapeutic response is well known in the art and applicants drew an analogy to the use of chemotherapy. However, examiner does not agree that this analogy holds, in view of that which is argued herein. Applicants have argued that the art is not unpredictable and referred examiner to two publications by Nemunaitis, J. et al. and Cavazanna-Calvo, M. et al. Nemunaitis et al. teach the administration of adenoviral vectors to the tumors of patients with non-small cell lung cancer and Cavazanna-Calvo et al. teach

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the treatment of SCID in children. Examiner argues that the two references cited were only directed to a specific cancer and the other to SCID. Applicant's also contend that the treatment of cancer via gene therapy has reached the point at which it is not unpredictable. Examiner however contests this statement and maintains that cancer gene therapy is unpredictable in view of the teachings set forth in the specification. In support of this the following review article is included. Gomez-Navarro, J. et al. in their review on Gene Therapy for Cancer in June 1999, state that the spontaneous behavior of human tumors is somewhat different from that of malignant cells *in vitro*, and from that of experimental tumors in animal models. (See Table 1, page 868, #7). Gomez-Navarro et al. also stated that major problems remain to be solved before these approaches can become effective and common place strategies for cancer. In view of the state of the art, the guidance set forth, the unpredictability in the art, one of skill in the art would require undue experimentation to use the instant invention as claimed for therapy. As such claims 10 and 11 stand rejected.

Further, it is pointed out that claim 10 depends upon claim 1 which does not recite what the heterologous gene is. Certainly, not just any gene could be used to treat cancer.

4. Claims 7-9 stand rejected under 35 USC § 112, first paragraph for reasons of record. Applicant's arguments have been fully considered but they are not persuasive. Claims 7-9 are drawn to cells comprising adenoviral vectors, and as such read on *in vivo* applicability. As stated above, applicants are not enabled for *in vivo* applicability

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due to the unpredictability in the art, and therefore stand rejected. Applicants however, are enabled for the following if the claims are amended such that they are not directed to *in vivo* applications. The claims could be amended to read as follows: 1) "An isolated cell comprising said adenoviral vector of claim 1"; or 2) "A cultured cell comprising said adenoviral vector of claim 1."

5. Claim 1 is rejected under 35 USC § 112, second paragraph for being indefinite. Claim 1 recites the term "essentially", which renders the claim indefinite.

Claim Rejections - 35 USC § 102

6. Claims 1-3, 5-10, 12-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Bischoff, J. et al. (US Patent NO: 6,080,578).

The claims are directed to recombinant vectors, adenoviruses or plasmids comprising an E1B deletion but still retaining the E1B promoter, comprising the following deletions pΔE1B, pΔE1B/55K and pΔE1B/pIX.

Bischoff et al. taught viruses comprising E1B gene deletions especially in the p55 region, but retaining the promoter. (See col. 4 lines 32-40). The mutant viruses taught by Bischoff exhibited a replication competent phenotype in neoplastic cells. (See abstract). Bischoff et al. also taught that the preferential killing of the neoplastic cells resulted either directly or by the expression of a cytotoxic gene in cells. (See abstract). Bischoff et al. also taught the construction of plasmids comprising several E1B

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deletions and deposited at the ATCC repository. (See claims 4, 5 and 6 , col. 25 and 26).


Claims 1-3, 5-10, 12-14 are rejected as anticipated by Bischoff et al.

Conclusion

7. Claims 1-3, 5-14 stand rejected.
8. Claim 4 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.
9. Any inquiry concerning this communication should be directed to Eleanor Sorbello, who can be reached at (703)-308-6043. The examiner can normally be reached on Mondays-Fridays from 6.30 a.m. to 3.00 p.m. EST.

Questions of formal matters can be directed to the patent analyst, Tracey Johnson, whose telephone number is (703) 305-2982.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


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